
Cellular postconditioning: allogeneic cardiosphere-derived cells reduce infarct size and attenuate microvascular obstruction when administered after reperfusion in pigs with acute myocardial infarction.

Journal: Circ Heart Fail

Publication Year: 2015

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PubMed link: 25587096

Funding Grants: Mechanism of heart regeneration by cardiosphere-derived cells

Public Summary:

Intracoronary delivery of cardiosphere-derived cells (CDCs) has been demonstrated to be safe and effective in porcine and human chronic myocardial infarction. However, intracoronary delivery of CDCs after reperfusion in acute myocardial infarction has never been assessed in a clinically-relevant large animal model. We tested CDCs as adjunctive therapy to reperfusion in a porcine model of myocardial infarction.

Scientific Abstract:

BACKGROUND: Intracoronary delivery of cardiosphere-derived cells (CDCs) has been demonstrated to be safe and effective in porcine and human chronic myocardial infarction. However, intracoronary delivery of CDCs after reperfusion in acute myocardial infarction has never been assessed in a clinically-relevant large animal model. We tested CDCs as adjunctive therapy to reperfusion in a porcine model of myocardial infarction. **METHODS AND RESULTS:** First, escalating doses (5, 7.5, and 10 million cells) of allogeneic CDCs were administered intracoronary 30 minutes after reperfusion. Forty-eight hours later, left ventriculography was performed and animals euthanized to measure area at risk, infarct size (IS), and microvascular obstruction. Second, identical end points were measured in a pivotal study of minipigs (n=14) that received 8.5 to 9 million allogeneic CDCs, placebo solution, or sham. Multiple indicators of cardioprotection were observed with 7.5 and 10 million allogeneic CDCs, but not 5 million CDCs, relative to control. In the pivotal study, IS, microvascular obstruction, cardiomyocyte apoptosis, and adverse left ventricular remodeling were all smaller in the CDC group than in sham or placebo groups. In addition, serum troponin I level at 24 hours was lower after CDC infusion than that in the placebo or sham groups, consistent with the histologically-demonstrated reduction in IS. **CONCLUSIONS:** Intracoronary delivery of allogeneic CDCs is safe, feasible, and effective in cardioprotection, reducing IS, preventing microvascular obstruction, and attenuating adverse acute remodeling. This novel cardioprotective effect, which we call cellular postconditioning, differs from previous strategies to reduce IS in that it works even when initiated with significant delay after reflow.

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